CBER Update

FDLI

December 10, 1996
Washington, DC

Kathryn C. Zoon, Ph.D.

Director, Center for Biologics Evaluation and Research

CBER UPDATE

- **Organizational Update**
- **CBER Workload and Performance**
- **Strategic Plan: The New Managed Review Process**
- **Reinvention Initiatives**
- **FY97 Priorities**

CBER UPDATE

- **Organizational Update**
- **CBER Workload and Performance**
- **Strategic Plan: The New Managed Review Process**
- **Reinvention Initiatives**
- **FY97 Priorities**

Quality Assurance Program

Joy Cavagnaro, Ph.D. (Acting)

Quality Assurance Staff

- Monitors the quality assurance and consistency of all CBER review activities.
- Provides oversight for CBER technical committees created to support review activities (i.e. Clinical Hold Committees, Refuse to File Committee.)
- Performs quality control functions to ensure accuracy of review and tracking of application data collected and reported by CBER.

Quality Assurance Staff

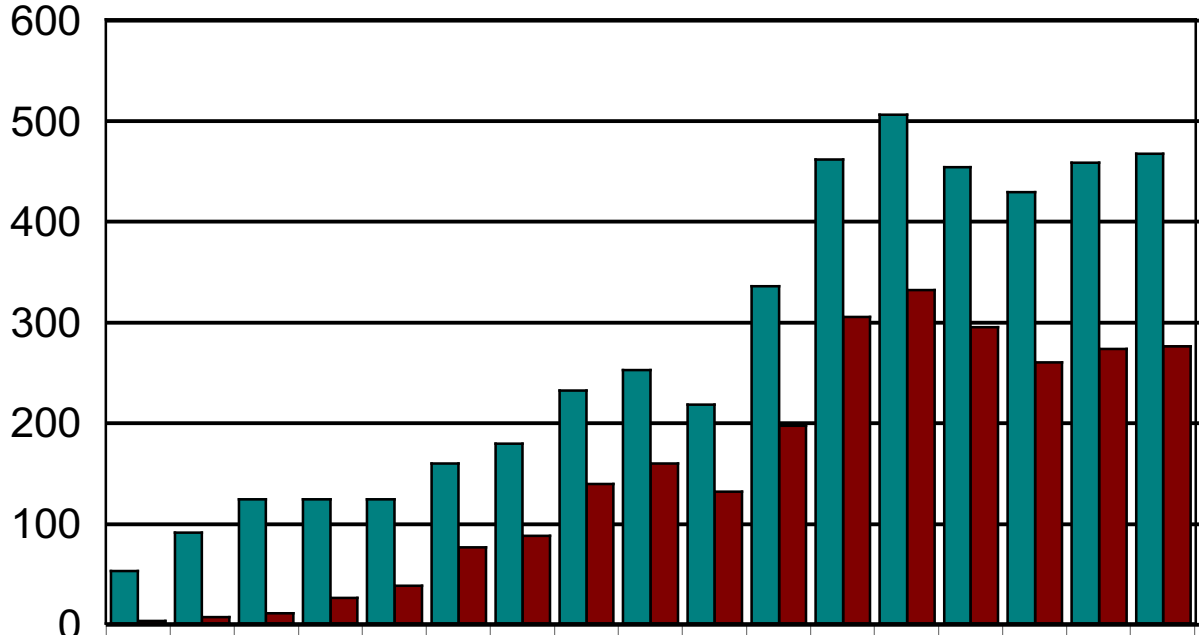
- Provides resolution of product jurisdiction concerns emanating from inside and outside CBER.
- Serves as Center liaison for resolution of review activity disputes unresolved at the division or office level between individuals or entities inside and outside of CBER.

CBER UPDATE

- **Organizational Update**
- **CBER Workload and Performance**
- **Strategic Plan: The New Managed Review Process**
- **Reinvention Initiatives**
- **FY97 Priorities**

CBER Biotech INDs/IDEs Received FY 80-96

Compared to Total



	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96
Total INDs/IDEs Received	52	90	123	123	123	159	178	231	251	217	335	460	505	453	428	457	466
Biotech INDs/IDEs	2	6	10	25	37	75	87	138	159	131	196	304	331	294	259	272	275

BIMS Data

dtb 10/9/96

CBER Product License Applications Received
FY92 - FY96

Fiscal Year	Total (All)	Blood/S.P.	Biotechnological Products				Other*
			Total	Therapeutic	Vaccine	In Vitro Diagnostics	
FY92	30	12	12	3	0	9	6
FY93	42	23	9	4	0	5	10
FY94	33	24	2	2	0	0	7
FY95	52	30	7	4	1	2	15
FY96	37	19	8	6	0	2	10

* Other includes Non-Biotech Vaccines, Therapeutics, Allergenics, and In Vitro Diagnostics

Data as of 30 September 1996/RIMS

CBER Review Performance
FY 94 Cohort of User Fee Applications*

Application Type	Number				Percent of First Actions	
	Submitted	Filed	AP	RTF, UN, or WF	Within Goal	Overdue
Establishment	8	5	0	3	100	0
New Product	8	5	1	3	100	0
Effectiveness Supp.	8	6	0	2	83	17
Manufacturing Supp.	195	186	98	9	85	15
Resubmission	100	N / A	72	N / A	92	6

AP = Approved, RTF = Refuse To File, UN = Unacceptable for Filing, WF = Withdrawn before Filing

* Data as of 31 October 1996/RIMS

CBER Review Performance
FY 95 Cohort of User Fee Applications*

Application Type	Number				Percent of First Actions	
	Submitted	Filed	AP	RTF, UN, or WF	Within Goal	Overdue
Establishment	9	8	3	1	100	0
New Product	15	14	7	1	100	0
Effectiveness Supp.	10	10	2	0	90	0
Manufacturing Supp.	270	269	185	1	94	6
Resubmission	80	N / A	52	N / A	84	3

AP = Approved, RTF = Refuse To File, UN = Unacceptable for Filing, WF = Withdrawn before Filing

* Data as of 31 October 1996/RIMS

CBER Review Performance
FY 96 Cohort of User Fee Applications*

Application Type	Number				Percent of First Actions	
	Submitted	Filed	AP	RTF, UN, or WF	Within Goal	Overdue
Establishment	10	10	3	0	50	0
New Product	14	13	3	1	38	0
Effectiveness Supp.	7	7	1	0	29	0
Manufacturing Supp.	262	262	139	0	65	2
Resubmission	18	N / A	6	N / A	50	0

AP = Approved, RTF = Refuse To File, UN = Unacceptable for Filing, WF = Withdrawn before Filing

* Data as of 31 October 1996/RIMS

Product License Applications

Average/Median (Months) Review Time To Approval
Excludes Merger/Corporate Entity Change
User Fee vs Non User Fee

Cohort Year Received	User Fee Avg./Median	Non User Fee Avg./Median
FY'93	24/22	18/15
FY'94	11/11	14/14
FY'95	9/11	9/9

Data as of 31 October 1996/RIMS

CBER

Some Major CBER Approvals - FY96

- ***Interferon beta-1a (Avonex)*** **- For treatment of multiple sclerosis (Orphan Indication) - May 17, 1996**
- ***Respiratory Syncytial Virus Immune Globulin Intravenous (Human) (Respigam)*** **- For prevention of serious lower respiratory tract infection in children less than 24 months of age with bronchopulmonary dysplasia - January 18, 1996**
- ***Nofetumomab (Verluma)*** **- Radiolabeled monoclonal antibody for detection of extensive disease in small cell lung cancer - August 20, 1996**

Some Major CBER Approvals - FY96

- ***HIV-1 p24 ELISA*** **- Screening and neutralization tests for detection of antibodies to HIV - March 14, 1996**
- ***HIV-Type 1 (Calypte HIV-1 Urine EIA)*** **- Screening kit used in the detection of antibodies to the HIV present in urine - August 6, 1996**
- ***HIV-1 Western Blot Kit*** **- For home use HIV testing using dried blood spot - used with the Confide Test Service -D.A.D. - July 22, 1996**
- ***HIV-1 PCR (Amplicor)*** **- Invitro Nucleic acid amplification test for (HIV-1) RNA in human plasma for use in disease prognosis - June 3, 1996**

Some Major CBER Approvals - FY96

- ***Hepatitis A Vaccine Inactivated (VAQTA) - For the active immunization of individuals ages 2 and older - March 29, 1996***
- ***Diphtheria & Tetanus Toxoids & Acellular Pertussis Vaccine Adsorbed (Tripedia)* - Primary immunization of infants - July 31, 1996**

Some Major CBER Approvals - FY96

- *Alteplase (Activase)* - Management of acute ischemic stroke - June 18, 1996
- *Interferon alfa-2 (Roferon-A)* - Treatment of chronic myclogenous leukemia - October 19, 1995
- *Interferon alfa-2 (Intron A)* - Adjuvant to surgery in patients with malignant melanoma - December 5, 1995

CBER UPDATE

- **Organizational Update**
- **CBER Workload and Performance**
- **Strategic Plan: The New Managed Review Process**
- **Reinvention Initiatives**
- **FY97 Priorities**

Strategic Goals

- A managed and integrated regulatory process from discovery through post marketing
- A high quality research program which contributes directly to the regulatory mission
- A high quality and diverse work force
- Interactive information systems which are integral to all CBER activities
- Leveraged resources

Goal: A managed and integrated regulatory process which is continuous from discovery through post-marketing

- **Strategies:**
  - **Apply the concepts of managed review to the entire regulatory process**
  - **Continually improve the regulatory process**
  - **Assure an accountable management that promotes teamwork at all staff levels**

PROJECT PLAN

- DEVELOP A BUSINESS MODEL OF CBER'S REGULATORY PROCESS
- IDENTIFY WEAKNESSES/BOTTLENECKS IN THE CURRENT REGULATORY PROCESS
- PROPOSE AND EVALUATE SOLUTIONS TO OVERCOME THESE WEAKNESSES/ BOTTLENECKS
- DESIGN A NEW, IMPROVED MRP
- IDENTIFY PERFORMANCE GOALS IN ORDER TO EXPAND THE MRP

CBER UPDATE

- **Organizational Update**
- **CBER Workload and Performance**
- **Strategic Plan: The New Managed Review Process**
- **Reinvention Initiatives**
- **FY97 Priorities**

REGO IIa

Allow ELA and PLA to be filed at different times.

- Published, July 10, 1995. FDA Guidance Document Concerning Use of Pilot Manufacturing Facilities for the Development and Manufacture of Biological Products; Availability

Licensure of pilot plants

- Published, July 10, 1995. FDA Guidance Document Concerning Use of Pilot Manufacturing Facilities for the Development and Manufacture of Biological Products; Availability

REGO IIa

Manufacturing changes-

Phase I - define categories of changes currently needing to be reported or not to be reported

- Published, April 6, 1995. Changes to be reported for Product and Establishment License Applications; Guidance

Phase II - Further define changes which need not be reported

- Proposed revision of §601.12 & NOA for 2 guidance documents published January 29, 1996. (61FR2739). Public Meeting held April 19, 1996. Comment Period closed May 6, 1996. Final rule in preparation.

Proposed Rule: Changes to an Approved Application

- 3 reporting categories of changes for product, production process, equipment, facilities or responsible personnel (21 CFR 600, 601, 314)
- 3 reporting categories of changes for package and container label and package insert (21 CFR 600, 601)
- Changes to advertising and promotional labeling must be in accordance with 21 CFR 314.81(b)(3)(i)

REGO IIa

- **Allow more prominence of distributor name on product labels**
  - **Final rule - §601.64 - Prominence of Name of Distributor of Biological Products, published November 6, 1996.**
- **Environmental Assessment for human drugs and biologics**
  - **Proposed Rule published 4/3/96**

REGO IIb

Elimination of the ELA requirement for Specified Biotechnology Products

- Final rule - Elimination of Establishment License Application for Specified Biotechnology and Specified Synthetic Biological Products - Published May 14, 1996.

Eliminate Lot Release for Specified Biotechnology Products

- Letters sent to manufacturers November 9, 1995. Policy published October 25, 1995 (60FR54695).

SCOPE OF THE FINAL ELA RULE

- **Therapeutic DNA Plasmid Products**
- **Therapeutic Synthetic Peptide Products**
  - **< 40 Amino Acids**
- **Monoclonal Antibody Products**

  For *In Vivo* Use
- **Therapeutic Recombinant DNA - Derived Products**

FINAL ELA RULE

- Eliminate Submission of an Establishment License Application
- Specified Biotechnology Products are Exempted from Certain Product Standards in 21 CFR Part 600
- Expands the Definition of Manufacturer

REGO IIb

Development of a Harmonized Application Form (HAF)

- Availability of Interim HAF published May 14, 1996. 60 day notice for final HAF (revised 356h) published October 1, 1996.

Eliminate the pre-approval requirement for promotional labeling and advertising

- Implemented immediately (November 9, 1995) Advertising and Promotional Labeling Staff Procedural Guide undergoing revision.

REGO IIb

- **Agency response to data submitted regarding clinical hold (respond in 30 days)**
  - Notice of availability of CBER & CDER SOPs re: clinical hold signed out of CBER October 4, 1996.
- **Revise requirement for a Responsible Head**
  - Proposed rule - Revised regulation concerning Responsible head signed out of CBER October, 1996.

Non-REGO

- **Line by line review of regulations (Part 600)**
  - Final rule - Revocation of Certain Regulations; Biological Products - published August 1, 1996.
- **Clarify data requirements for entering an unapproved drug or biologic into human studies**
  - Published January 24, 1996. Guidance for Industry; Content and Format of Investigational New Drug Applications (IND's) for Phase 1 Studies of Drugs, Including Well-characterized Therapeutic, Biotechnology-Derived Products.

Regulations Rewrite

- Major Initiatives
  - Single Application for all Biological Products
  - Revise Regulations to update or delete outmoded regulations

OTHER INITIATIVES in PROGRESS

- **Regulation of Tissue And Cellular Therapies**
- **Xenotransplantation**
- **Gene Therapy**
- **Blood Initiative**

CBER UPDATE

- **Organizational Update**
- **CBER Workload and Performance**
- **Strategic Plan: The New Managed Review Process**
- **Reinvention Initiatives**
- **FY97 Priorities**

CBER Priorities
FY97

- Meet or exceed the PDUFA FY 97 performance standards for reviewing applications for which fees are paid.
- Take whatever actions are necessary to assure the safety of, and public confidence in the Nation's blood supply.
- Facilitate the development and approval of significant vaccine, blood, and therapeutic product advances through review, policy formulation, regulation development, guidance issuance to industry, workshops, and meetings.

CBER Priorities
FY97

- Pursue excellence in research that is directly targeted to the evaluation and regulation of biological products.
- Improve automated system support for the review and evaluation of biological products.
- Continue to support efforts for a high quality, diverse work force.

HOW TO GET INFORMATION FROM CBER

CONTACT THE OFFICE OF COMMUNICATION, TRAINING, AND MANUFACTURERS ASSISTANCE (OCTMA)

REQUEST DOCUMENTS THROUGH THE INTERNET!

SEND E-MAIL TO:

"CBER_INFO@A1.CBER.FDA.GOV"

FOR A LIST OF DOCUMENTS:

"DOC_LIST@A1.CBER.FDA.GOV"